IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Marvin J. Slepian		
Serial No.:	10/072,766	Art Unit:	1633
Filed:	February 8, 2002	Examiner:	Maria Marvich
For:	*ENDOMURAL THERAPY*		

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY BRIEF

Sir:

This is a Reply Brief to the Examiner's Answer mailed January 7, 2009, in the above-referenced application. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

A Supplemental Information Disclosure Statement (IDS) with one (1) page of Form PTO -1449 and copies of two (2) documents cited therein was filed under 37 C.F.R. § 1.97(d) along with payment of the required fee on March 19, 2008. Applicants respectfully request review of this IDS by the Examiner and return of the initialed Form PTO-1449.

(4) STATUS OF AMENDMENTS

The claims were last amended in an Amendment filed via facsimile transmission on November 13, 2007. This amendment was entered, as indicated in the Advisory Action mailed on December 12, 2007. An appendix to the Appeal Brief set forth the claims on appeal.

(6) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The Grounds of Rejection listed in the Appeal Brief included claims 4, 14 and 34 in the list of rejected claims. However these claims were canceled.

(a) Whether claims 1, 3, 6, 7, 15-18, 20-23, 25, 28, 29, 32 and 35-37 are disclosed under 35 U.S.C. § 102(e) by U.S. Patent No. 6,585,716 to Altman.

(b) Whether claims 1, 3, 6, 7, 15-19, 21-23, 25, 36 and 37 are disclosed under 35 U.S.C. §102(e) by U.S. patent No. 6,102,887 to Altman.

(c) Whether claims 1, 3, 6, 7, 15, 16, 18, 20-24, 32, and 35-37 are disclosed under 35 U.S.C. § 102(e) by U.S. Patent No. 6,309,370 to Haim, *et al.*

(d) Whether claims 13 and 33 are obvious under 35 U.S.C. § 103(a) in view of U.S. Patent No. 6,585,716 to Altman, U.S. Patent No. 6,102,887 to Altman or U.S. Patent No. 6,309,370 to Haim, et al. in view of Benjamin and McMillan, *Circ. Res.*, 83: 117-132 (1998).

(e) Whether claim 31 is obvious under 35 U.S.C. § 103(a) over Brosamle, *et al.*, *J. Neurosci.*, 20:21, 8061-8068 (2000) in view of U.S. Patent No. 6,585,716, Altman or U.S. Patent No. 6,102,887 to Altman or U.S. Patent No. 6,309,370 to Haim, *et al.*

(7) ARGUMENT

Appellants affirm all of the arguments made in the Appeal Brief.

The claims on appeal define devices, kits and methods for treatment of the endomural zone of an organ, organ component or tissue structure with minimal damage to surrounding tissue. The devices, kits and methods are directed at cutting or removing tissue from the endomural zone of an organ, organ component or tissue structure to create a new void or cavity and placing in the void or cavity a polymeric material. The claimed method also specifies that the polymeric material contains a therapeutic, prophylactic or diagnostic agent, which is locally delivered to the endomural zone.

The endomural zone is a particular area within an organ, organ component or tissue structure.

The endomural zone refers to "the middle zone", where most of the "business activity" for the organ occurs. The specification explains that if one views the cross-section of an organ, the ectoluminal zone may be characterized as the outer 10% ± 10 of the cross-sectional area, the endomural zone is the middle 80% ± 10 of the cross-sectional area, and the endoluminal zone is the inner 10% ± 10 of the cross-sectional area. (Specification, page 6, lines 12-15). With respect to tubular organs and tissue structures, the walls of the tubular structures have the same three zones, *i.e.* ectoluminal, endomural, and endoluminal. (Specification, page 6, lines 22-28).

The specification explains a number of advantanges that result when one practices the claimed method or uses the claimed devices and kits. First, the methods, devices and kits are designed to reduce damage to collateral healthy tissue, while removing, containing or locally treating active disease within the endomural regions of an organ, organ component or tissue structure. The claimed method is also designed to more effectively treat a disease locally with

therapeutic agents, such as pharmaceuticals or cells, while reducing the risk of systemic delivery of the therapeutic agent or cells. This targeted treatment allows application of higher effective concentration of agents without fear of toxicities with reduced systemic spillover effects. (Specification, page 7, lines 6-17)

Further, by placing an agent directly in the endomural zone of an organ, the agent will be released more uniformly throughout the organ compared to placement of the agent on the periphery of the organ.

The claimed methods require the creation of a void, cavity, containment space or reservoir area in the endomural zone. The creation of such spaces within an organ allows "rebuilding" and reconstruction from inside. Placing therapeutic agents or materials in the endomural zone protects the agents or materials from overlying blood flow, increases retention and thereby sustains action of the agents. (Specification, page 7, lines 19-26)

Another advantage of the claimed methods, devices and kits is that they can be used to grown different types of cells in the endomural zone of an organ. As noted in the specification, following removal of tissue from the endomural zone, cells that are different from the cells that were removed can be placed in the void. In this embodiment, the organ can be used to grow cells to provide a function that is typically provided by another organ. This is particularly useful when a disease has diminished or destroyed a vital function of an organ. (Specification, page 8, lines 1-15). Appellants note, however, that dependent claims that are specifically directed to depositing cells in the endomural zone or a kit containing cells are currently withdrawn from consideration.

In contrast to the claimed methods, devices and kits, the prior art cited by the Examiner does not disclose delivery of an agent directly to the endomural zone of an organ. The '716 patent and the '887 patents disclose controlled deployment of needles to "a depth" within tissue. However, the site of delivery within the tissue is not described in these patents. For example, neither the '716 nor the '887 patent describe a preference for a particular area within the myocardium.

Additionally, none of the references cited by the Examiner describes cutting or removing tissue, as required by the method claims or a device that contains a means for creating a void, cavity, containment space or reservoir area, as required by the device and kit claims.

(i) Rejections Under 35 U.S.C. § 102

(1) Claims 1, 3, 6, 7, 15-18, 20-23, 25, 28, 29, 32 and 35-37 are not anticipated by U.S. Patent No. 6,585,716 by Altman ("the '716 patent").

Claims 1, 3, 6, 7, and 35-37 are novel over the '716 patent

Independent claim 1 requires in part: (1) penetrating into the endomural zone of an organ, organ component or tissue structure and (2) cutting or removing tissue in the endomural zone to create a void, cavity, containment space or reservoir. Thus, these two steps are separate steps in the claimed method.

The '716 patent discloses extending a curved or helical needle from the distal tip of the device and penetrating the wall of the vein so the needle enters the myocardium (*see* col. 4, lines 14-19 and col. 5, lines 32-34). The '716 patent does not disclose a separate step of cutting tissue or of removing tissue, as required by independent claim 1 and its dependent claims.

Additionally, the '716 patent refers to delivery of a therapeutic substance "to a depth within the heart muscle" (*see* col. 5, lines 61-63), but never specifies the location or depth within the myocardium to which the therapeutic substance is delivered. As noted above, the heart has three zones, *i.e.* the ectoluminal, endomural, and endoluminal zones. Thus, a reference to administration to "a depth" in the heart tissue does not amount to a disclosure of delivering to a particular zone within the myocardium, namely the endomural zone, as required by claim 1 and its dependent claims.

For at least the reasons discussed above and in the Appeal Brief, claims 1, 3, 6, 7, and 35-37 are novel over the '716 patent.

Claims 15-18 and 20-23 are novel over the '716 patent

Independent claim 15 defines a device, which requires in part: (1) a hollow tubular member with (a) an end means for creating a void, cavity, containment space or reservoir area in the endomural zone of an organ, organ component or tissue structure, by cutting or removal of tissue, and (2) means for local delivery of a therapeutic, prophylactic or diagnostic agent into the void cavity, containment space or reservoir area. Thus the means for creating a void, cavity, containment space or reservoir area is a separate element from the means for local delivery of a therapeutic, prophylactic or diagnostic agent.

The '716 patent discloses a device containing a drug delivery catheter (element 22), which contains a penetrating element (*e.g.* a curved or helical needle) (element 28) at its distal end; the penetrating element is used to deliver a therapeutic agent (*see e.g.* Figures 1 and 2 and col. 4, lines 5-19 and 50-61). The '716 patent does not disclose a separate element that is a

means for creating a void, cavity, containment space or reservoir area. Thus, even if the needle disclosed in the '716 patent was capable of creating a void, as asserted by the Examiner in the Examiner's Answer at page 4, the device in the '716 patent would still be structurally different from the claimed device since the device in the '716 patent does not contain one element for delivery of an agent and a separate element for creating a void. Further, as noted in the Appeal Brief, the device disclosed in the '716 patent does not contain an element that is able to cut or remove tissue, as required by claim 15 and its dependent claims. For example, if the penetrating element (element 28) cut or removed tissue, the tissue would clog the needle and prevent the delivery of the therapeutic.

For at least the reasons discussed above and in the Appeal Brief, claims 15-18 and 20-23 are novel over the '716 patent.

Claim 21 is novel over the '716 patent

In addition to the reasons discussed in the Appeal Brief and above with respect to independent claim 15, dependent claim 21 is novel over the '716 patent for at least the following additional reason. The '716 patent does not disclose including a projectile means to ballistically transfer particles through the ectoluminal or endoluminal zone for retention in the endomural zone, as required by the device defined by claim 21. Therefore claim 21 is novel over the '716 patent.

Claims 25, 28, 29, and 32 are novel over the '716 patent

Independent claim 25 defines a kit requiring, in part: a device containing a means for creating a void, cavity, containment space or reservoir area in the endomural zone and a means

for local delivery of therapeutic, prophylactic or diagnostic agents into the void, cavity, containment space or reservoir area, and a void filling polymeric material or implant in a form suitable for local delivery.

The device disclosed in the '716 patent only contains a drug delivery element and does not contain an element for creating a void, cavity, containment space or reservoir area. Further, the '716 patent does not disclose a void filling polymeric material or implant in a form suitable for local delivery. Col. 6, lines 8-39 of the '716 patent describes problems associated with various controlled release systems and notes that prior art systems could migrate from the heart and travel to the brain and other organs (col. 6, lines 13-16). The '716 patent notes that its method is superior to the prior art since the approach is through the venous side, thereby preventing embolic events in the arteries, "even if a large portion of the injected microspheres wash out of the delivery site" (col. 6, lines 29-36). Thus, the '716 patent only describes injection of polymeric microspheres that are capable of washout from the injection site. These microspheres are not a void filling material in a form suitable for local delivery, as required by independent claim 25. For at least the reasons discussed above and in the Appeal Brief, claims 25, 28, 29, and 32 are novel over the '716 patent.

(2) Claims 1, 3, 6, 7, 15-19, 21-23, 25, 36 and 37 are not anticipated by U.S. Patent No. 6,102,887 by Altman ("the '887 patent").

Claims 1, 3, 6, 7, 36 and 37 are novel over the '887 patent

The '887 patent discloses advancing a penetrating element to cause it to penetrate the endocardium and injecting an anti-arrhythmic drug or pro-rhythmic drug deep into the

myocardium through the penetrating element (col. 3, lines 22-26). The '887 patent does not disclose a separate step of cutting tissue or of removing tissue to form a void, cavity, containment space or reservoir area, as required by independent claim 1 and its dependent claims.

The Examiner points to col. 9, lines 22-44 in support of her rejection. (Examiner's Answer pages 6 and 12). However, as noted in the Appeal Brief, the '887 patent does not disclose the step of cutting or removing tissue to form a void, cavity, containment space or reservoir area, as required by independent claim 1. Rather, the '887 patent describes ***stabilizing*** the penetrating element using the "prong fixation system" described in Figure 8a-8c and col. 9, line 21 until col. 10, line 26. The prong fixation system merely pierces the tissue with the prong structures. Contrary to the Examiner's assertion, the prongs do not inherently create a void when they spread the tissue. (Examiner's Answer, page 6) Creating a void between the prongs, as suggested by the Examiner, would eviscerate the selected penetration site, rather than stabilize it. Additionally, the '887 patent discloses that the prongs may be made of a softer, more blunt structure so that they do not penetrate the tissue, and still accomplish the function of stabilizing the target penetration site. (col. 9, lines 44-47). Thus, there is no disclosure in the '887 patent to cut or remove tissue to form a void, cavity, containment space or reservoir area.

Additionally, the '887 patent refers to delivery of a therapeutic substance "deep into the myocardium" (*id.*) or "to a depth" within tissue (*see* col. 6, lines 45-46), but never specifies the location or depth within the myocardium to which the therapeutic substance is delivered. As noted above, the heart has three zones, *i.e.* the ectoluminal, endomural, and endoluminal zones.

Thus, a reference to administration to "a depth" in the tissue does not amount to a disclosure of delivering to the endomural zone, as required by claim 1 and its dependent claims.

For at least the reasons discussed above and in the Appeal Brief, claims 1, 3, 6, 7, and 35-37 are novel over the '887 patent.

Claims 15-18 and 20-23 are novel over the '887 patent

The '887 patent discloses a device containing a steerable catheter. In one embodiment, the device includes an expanding prong fixation system. As noted above, the prong fixation system is able to pierce tissue to stabilize the tissue surrounding the target site and thereby stabilize the penetration element. However, the prong fixation system does not cut or remove tissue, nor is it able to create a void, cavity, containment space or reservoir area, as required by claim 15. Further, the penetrating element (*e.g.* a curved or helical needle) (*e.g.* element 30) is designed to deliver a therapeutic agent. The penetrating element cannot also cut or remove tissue since the tissue would clog the needle and prevent the delivery of the therapeutic.

For at least the reasons discussed above and in the Appeal Brief, claims 15-18 and 20-23 are novel over the '887 patent.

Claim 19 is novel over the '887 patent

In addition to the reasons discussed in the Appeal Brief and above with respect to independent claim 15, dependent claim 19 is novel over the '887 patent for at least the following additional reason. The '887 patent does not disclose including an expansile cutter attached to the end of the tubular member, as required by the device defined by claim 21. Therefore claim 19 is novel over the '887 patent.

Claim 21 is novel over the '887 patent

In addition to the reasons discussed in the Appeal Brief and above with respect to independent claim 15, dependent claim 21 is novel over the '887 patent for at least the following additional reason. The '887 patent does not disclose including a projectile means to ballistically transfer particles through the ectoluminal or endoluminal zone for retention in the endomural zone, as required by the device defined by claim 21. Therefore claim 21 is novel over the '887 patent.

Claims 25, 28, 29, and 32 are novel over the '887 patent

Independent claim 25 defines a kit requiring, in part: a device containing a means for creating a void, cavity, containment space or reservoir area in the endomural zone and a means for local delivery of therapeutic, prophylactic or diagnostic agents into the void, cavity, containment space or reservoir area, and a void filling polymeric material or implant in a form suitable for local delivery.

As noted above, the device disclosed in the '887 patent does not contain an element for creating a void, cavity, containment space or reservoir area. Further, the '887 patent does not disclose a void filling polymeric material or implant in a form suitable for local delivery. From Col. 10, line 58 until col. 12, line 60, the '887 patent describes a variety of different therapeutic that can be injected into the heart. However, the '887 patent does not disclose a void filling material (possibly since no void has been formed) or implant in a form suitable for local delivery. For at least the reasons discussed above and in the Appeal Brief, claims 25, 28, 29, and 32 are novel over the '887 patent.

(3) Claims 1, 3, 6, 7, 15, 16, 18, 20-24, 32 and 35-37 are not anticipated by U.S. Patent No. 6,309,370 by Haim, *et al.* ("the '370 patent").

Claims 1, 3, 6, 7, 35- 37 are novel over the '370 patent

The '370 patent discloses a method for delivering therapeutic agents, such as growth factors, to the heart. The '370 patent focuses on coordinating the drug delivery with a viability map of the heart to ensure that the drug is only administered to ischemic, but still viable, regions of the heart (*see* col. 13, line 16 until col. 14, line 2). In contrast to claim 1, the method described in the '370 patent does not require cutting or removing tissue. As noted above with respect to the '617 and 887 patents, if tissue was cut or removed by the needle (element 24), then the tissue would clog the needle and prevent the delivery of the therapeutic agent. Further, the '370 patent is concerned with preventing materials from entering the distal end of the catheter and needle. For example, the '370 patent explains that the device includes a seal (element 28), which prevents back-flow of blood into the sheath and the catheter (*see* col. 11, lines 32-43).

The '370 patent discloses that preferably the needle extends 2-3 mm beyond the tip of the distal end of the catheter (col. 11, lines 29-31). Using such a depth would result in shallow delivery of the therapeutic agent to the myocardium.

For at least the reasons discussed above and in the Appeal Brief, claims 1, 3, 6, 7, and 35-37 are novel over the '370 patent.

Claims 15-18 and 20-23, 25, 28, 29, and 32 are novel over the '370 patent

The '370 patent discloses a device containing a drug delivery catheter (element 20), which contains a hollow needle (element 24) at its distal end; the needle is used to deliver a

therapeutic agent (*see e.g.* Figures 1A and 1B and col. 11, 9-19). The needle does not create a void, cavity, containment space or reservoir area, as required by the device defined in independent claim 15. For example, if the needle (element 20) cut or removed tissue, the tissue would clog the needle and prevent the delivery of the therapeutic.

For at least the reasons discussed above and in the Appeal Brief, claims 15-18, 20-23, 25, 28, 29 and 32 are novel over the '370 patent.

For the at least the reasons set forth in the Appeal Brief and above, Appellants submit that claims 1, 3, 6, 7, 13, 15-25, 28-33, and 35-37 are patentable.

Respectfully submitted,

/Rivka D. Monheit/
Rivka D. Monheit
Reg. No. 48,731

Date: March 9, 2009

PABST PATENT GROUP LLP
1545 Peachtree Street, NE
Suite 320
Atlanta, Georgia 30309
(404) 879-2152
(404) 879-2160 (Facsimile)